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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,598	06/30/2003	Johannes B.M.M. Van Bree	4064.1000-005	2502

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EXAMINER	
DAVIS, RUTH A	
ART UNIT	**PAPER NUMBER**
1651	

MAIL DATE	DELIVERY MODE
05/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/611,598	VAN BREE ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's Request for Continued Examination, amendment and response filed on March 5, 2007 have been received and entered into the case. Claims 36, 38, 40, 43, 56 – 58 and 65 – 67 are canceled; claim 1 is pending and has been considered on the merits. All arguments have been fully considered.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Reuser et al. (US 6118045), Van Hove et al. (Proc Natl Acad Sci, Vol.93, p.65-70, Jan 1996, Genetics), and Kikuchi et al. (J Clin Invest, Vol.101, Num.4, Feb 1998, p. 827-833).

Applicant claims a method for treating a human with Pompe's disease, the method comprising intravenously administering biweekly to the patient a therapeutically effective amount of human alpha glucosidase, whereby the concentration of accumulated glycogen in the patient is reduced and/or further accumulation of glycogen is arrested.

Reuser teaches that patients with deficiencies resulting in insufficient function of lysosomal enzyme (i.e. Pompe's disease) (col.1 line 53-56) can be treated by administering exogenous enzymes to the patient (col.10 line64 – col.11 line 5). Reuser teaches the compositions can be typically administered intravenously (col.11 line 58-61) and are administered in amounts sufficient to reduce the concentration of accumulated metabolites (glycogen) and/or arrest further accumulation of the metabolite (glycogen).

Van Hove teaches in vivo administration of alpha-glucosidase wherein intracellular glycogen dropped to normal levels (p.68, Correction of Patient's Fibroblasts). Specifically, Van Hove teaches intravenously administering alpha-glucosidase to a patient (table 4) and that an effective therapy includes uptake of the enzyme by the cells and a decrease in accumulation of glycogen (p.69, right col, para 1). Van Hove concludes that decreases in glycogen levels as a result of the intravenous enzyme administration is a treatment for Pompe's disease and suggests human alpha glucosidase for such treatment (p.69, right col, para 1).

Kikuchi teaches IV administration of human alpha glucosidase results in reduced glycogen levels and that such administration is a therapy for human Pompe's Disease (abstract).

Kikuchi teaches administration every few days over an 18 day period, that the response is dose dependent, and that intermediate doses extended treatment and halted progression of the disease (abstract).

Although none of the reference specifically teach a method for treating Pompe's disease by administering alpha glucosidase biweekly, the references clearly demonstrate to one in the art that IV administration of alpha glucosidase to a patient with Pompe's disease is an effective treatment which results in reduced glycogen accumulation as well as arresting further accumulation of glycogen. All of the references explicitly suggest that IV administration of alpha-glucosidase to a human would be an effective treatment. In addition, Kikuchi demonstrates that regular administration extends therapeutic value and may halt progression of Pompe's disease. At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to administer alpha-glucosidase intravenously to a patient with Pompe's disease because of the known activities of reducing glycogen accumulation and arresting further glycogen accumulation, as evidenced by the cited references. It would have been further obvious to one of ordinary skill in the art to optimize the specific dosage amounts and frequencies, as a matter of routine experimentation, since the art clearly teaches that such variables are key to treating and ultimately halting the disease. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by the cited references to treat a human via IV administration of alpha-glucosidase and optimize the dose and administration cycles, with a reasonable expectation for successfully treating Pompe's disease.

Response to Arguments

Applicant argues that the references do not teach improvement after a single dose, that replacement therapy works, that Pompe's disease can be treated with alph-glucosidase, that the glycogen levels are reduced, or the therapeutic effects as claimed. Applicant additionally argues that references do not teach treating a human, or administering in the manner as claimed and that the art only teaches failed attempts of replacement enzymes. Applicant further argues that there is not a motivation to combine the references, there is not a motivation to treat Pompe's disease, that there is no expectation of success and that the examiner uses improper hindsight.

However, these arguments fail to persuade because as evidenced by the cited references, the prior art clearly teaches in vivo evidence of improvement and effective treatment of Pompe's disease by IV administration of alpha-glucosidase. The art clearly teaches that glycogen levels are reduced and that further accumulation of glycogen is arrested as claimed. While the art does not specifically teach administration to a human, the art clearly demonstrates the method of administering alpha-glucosidase to an individual with deficiencies resulting in insufficient function of lysosomal enzyme (i.e. Pompe's disease) results in successful treatment and halting of the progression of the disease. Thus, the prior art clearly suggests and provides factual, animal based evidence that deficiencies resulting in insufficient function of lysosomal enzyme (i.e. Pompe's disease) can be treated with IV administration of alpha-glucosidase. Moreover, in following the teachings of the prior art, one in the art would have been motivated by the cited references and routine experimentation, to optimize the specific dose requirements of the enzyme and to intravenously administered alpha-glucosidase to a human with a reasonable expectation for successfully treating Pompe's disease.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 571-272-0915. The examiner can normally be reached on M-F 7:00 -3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ruth A. Davis/
Primary Examiner
Art Unit 1651

May 25, 2007